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Bone Union of Osseous Microvascular Free Tissue Transfer in Mandibular Reconstruction

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Abstract

Objectives. Osseous microvascular free tissue transfer (MFTT) is the gold standard for reconstruction for most segmental mandibulectomy defects. The most common osseous MFTT utilized in reconstruction is the fibular, scapular, and osteocutaneous radial forearm (OCRF) free flap. We evaluated postoperative bone union as well as clinical complications following MFTT and the impact of various patient and reconstructive characteristics, including type of osseous MFTT.

Study Design. Retrospective cohort study.

Setting. Tertiary care academic hospital.

Methods. This study examined patients who underwent osseous MFTT for mandibular defects from January 2017 to January 2019.

Results. An overall 144 osteotomies in 58 patients were evaluated. Of the 144 junctions, 28 (19.4%) showed radiographic nonunion. Patients who underwent preoperative (odds ratio [OR] = 0.30, *P* = .027) and postoperative (OR = 0.28, *P* = .003) radiation had a significantly lower bone union score. Time from surgery to postoperative imaging was associated with higher bone union scores (OR = 1.07, *P* = .024). When bone union scores were compared among types of MFTT, fibular (OR = 5.62, *P* = .008) and scapular (OR = 4.69, *P* = .043) MFTT had significantly higher scores than OCRF MFTT. Twelve (20.7%) patients had postoperative complications. There was no statistically significant correlation between clinical complications and various variables, including type of osseous MFTT.

Conclusion. Pre- and postoperative radiation and time from surgery have an impact on bone union. Regarding the type of MFTT, fibular and scapular MFTT appeared to have higher bone union when compared with OCRF. There was no impact of bone union or type of osseous MFTT on clinical complications.

Keywords

bone union, microvascular free tissue transfer, segmental mandibulectomy

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Segmental resection of the mandible is frequently performed in head and neck surgery for the management of malignant and benign pathologies. Optimal reconstruction of the mandible must accomplish the goal of restoring mandibular continuity and function. Prior to the advent of microvascular surgery, nonvascularized and pedicled bone was used for mandible reconstruction with suboptimal outcomes. In the 1980s, various osseous free flaps were introduced and became the gold standard of mandibular reconstruction. These include fibular, scapular, iliac crest, and osteocutaneous radial forearm (OCRF) free flaps.[1,2]

Contouring bone in mandibular reconstruction can be challenging; osteotomies of the free flap bone are often required. These bone segments must directly oppose each other as well

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as the native bone. Nonunion or malunion can lead to poor functional and aesthetic outcome, although the literature to support this is lacking. Fibular free flaps have been the workhorse of mandibular reconstruction. Several studies have evaluated bony union following free fibular flap. Rates of bony union are >90% in a small number of studies that have explored this in mandibular reconstruction.[3-6]

In this study, we examined patients who underwent segmental mandibulectomies and mandibular reconstruction with microvascular free tissue transfer (MFTT). We analyzed postoperative computed tomography (CT) scans to assess the quality of bony union. We evaluated whether degree of bone union varied by the type of free flap in addition to other patient and surgical characteristics. We also examined the rates of postoperative complications and their association with bone union.

Materials and Methods

This retrospective study examined patients who underwent osseous free flap reconstruction for mandibular defects at our tertiary care academic hospital. The study was approved through The Ohio State University's Institutional Review Board (2019H0469). Patients who underwent an operative procedure from January 2017 to January 2019 were isolated. Inclusion criteria comprised malignant or benign disease and osseous free flaps, including fibular, scapula, or OCRF MFTT. Patients were required to have at least 1 postoperative visit as well as CT imaging at least 3 months following surgery. Patients were excluded if they did not have appropriate follow-up or imaging.

Medical information and imaging from the electronic medical records were reviewed. Demographic information was obtained, such as sex, age at time of surgery, sex, and history of smoking and alcohol use. Disease characteristics (location and pathology) were collected. Pre- or postoperative treatment with radiation and/or chemotherapy was recorded. Surgical data were obtained: date of surgery, type of osseous free flap (fibula, scapula, radius), and length and number of osteotomies. Postoperative clinic notes were reviewed to identify any postoperative complications associated with the mandibular reconstruction, such as hardware exposure, fistulas, or infections related to the mandible or mandibular hardware.

Evaluation of Bone Union

The most recent CT image visualizing the mandible was reviewed. CT imaging, with or without contrast, with 1-mm cuts was included where the entirety of the mandible was visualized. Each osteotomy was assessed independently. Evaluation of bone union was performed by 2 independent neuroradiologists. A scale of 0 to 2 was used to assess bone union in terms of callus formation, as done in similar studies[5]: 0, absent callus formation; 1, complete callus formation on the labial or lingual side; 2, complete callus formation on both the labial and lingual sides. Each bone-to-bone contact site was defined as an independent osteotomy. Bone segments described the number of fragments of the osseous free flap to reconstruct the mandible. Therefore, 1 bone segment would lead to 2 osteotomy sites, unless the bone was used to reconstruct the condyle. Osteotomy junction was categorized as being either between the patient's native bone and MFTT or between 2 bone segments of the MFTT.

The time from surgery to CT scan was determined from the date of the MFTT procedure to the most recent available CT scan. The laterality of the osteotomy site was designated as left, midline, or right based on the radiologists' assessments. The location of the osteotomy was designated as anterior or lateral, again based on the radiologists' analysis of the postoperative imaging. Anterior defined the symphyseal and parasymphyseal regions, and lateral included the body, angle, ramus, and condyle of the mandible.

Statistical Analysis

Patient characteristics were summarized via descriptive statistics—medians for the continuous variables and frequencies for the categorical variables—as well as by postoperative complication status. Cohen k coefficient was used to measure interrater agreement between 2 radiologists. Cohen k coefficient is often interpreted as follows: ≤0.2, poor; 0.21-0.40, fair; 0.41-0.60, moderate; 0.61-0.80, good; and >0.8, very good agreement.[7] To determine the association of predictors on bone union score, odds ratios (ORs) were calculated with ordinal generalized estimating equations that account for clustering by patients. A P value <.05 was considered statistically significant. All analyses were conducted with the SAS version 9.4 (SAS Institute Inc).

Results

A total of 58 patients underwent osseous MFTT and met the inclusion criteria during the period from January 2017 to July 2019. Patient demographic information is summarized in **Table 1**. The median age was 60 years. The patient cohort was 27.6% (n = 16) female and 72.4% (n = 42) male. Nonsmokers represented 32.8% (n = 19) of the patients, while 67.2% (n = 39) had a history of smoking. History of heavy alcohol use was reported in 43.1% (n = 25). The majority of pathology consisted of oral cavity squamous cell carcinoma (n = 40). The other pathologies were osteonecrosis (n = 13), ameloblastoma (n = 4), and sarcoma (n = 1).

History of preoperative radiation (n = 3), chemotherapy (n = 3), or chemoradiation (n = 7) was assessed. Forty-five patients had no history of preoperative radiation or chemotherapy. Adjuvant treatment included radiation (n = 9) and chemoradiation (n = 23). Twenty-six patients did not require postoperative adjuvant therapy. The presence of postoperative clinical complications was reviewed. Twelve patients (20.7%) had postoperative complications related to the mandible, such as exposed hardware, fistulas, osteoradionecrosis, and cellulitis or soft tissue infection.

The median time from surgery to most recent CT scan was 11.6 months. The median length of the segmental mandibulectomy was 7 cm. Osseous free flap types included fibular (n = 44, 75.9%), scapular (n = 8, 13.8%), and OCRF (n = 6, 10.3%) MFTT (**Table 1**). Selection of the MFTT was based

Table 1. Demographics of Patients Undergoing Osseous Microvascular Free Tissue Transfer (N = 58).

	Patients, No. (%)
Age, y, median (Q1, Q3)	60 (49, 68)
Sex	
Female	16 (27.6)
Male	42 (72.4)
Smoking	
No	19 (32.8)
Yes	39 (67.2)
Alcohol	
No	33 (56.9)
Yes	25 (43.1)
Preoperative radiation	
No	48 (82.8)
Yes	10 (17.2)[a]
Preoperative chemotherapy	
No	48 (82.8)
Yes	10 (17.2)[a]
Postoperative radiation	
No	26 (44.8)
Yes	32 (55.2)[b]
Postoperative chemotherapy	
No	35 (60.3)
Yes	23 (39.7)[b]
Length of osteotomy, cm, median (Q1, Q3)	7 (5, 8)
Clinical complication	
No	46 (79.3)
Yes	12 (20.7)
Free flap type	
Fibula	44 (75.9)
Scapula	8 (13.8)
Osteocutaneous radial forearm	6 (10.3)

[a]Seven patients had preoperative chemoradiation.
[b]Twenty-three patients had postoperative chemoradiation.

Table 2. Osteotomy Characteristics (N = 144).[a]

	Osteotomies, No. (%)
Time from surgery to CT scan, mo, median (Q1, Q3)	11.6 (5.9, 16.4)
Laterality	
Left	73 (50.7)
Midline	6 (4.2)
Right	65 (45.1)
Site	
Anterior	86 (59.7)
Lateral	58 (40.3)
Osteotomy junction	
Native bone and free flap	117 (81.2)
Between free flaps	27 (18.8)
Average bone union score	
0	28 (19.4)
0.5	12 (8.3)
1	61 (42.4)
1.5	15 (10.4)
2	28 (19.4)

Abbreviation: CT, computed tomography.
[a]A scale of 0 to 2 was used to assess bone union in terms of callus formation: 0, absent callus formation; 1, complete callus formation on the labial or lingual side; 2, complete callus formation on both the labial and lingual sides.

on several variables, such as length of anticipated bone and soft tissue defect, vascularity at the donor site, as well as dentition. Each osteotomy was assessed individually, totaling 144 osteotomies in 58 patients (**Table 2**). The number of bone segments included 1 (n = 32), 2 (n = 24), and 3 (n = 2). The 144 sites of bony union were characterized by laterality and site. Seventy-three (50.7%) osteotomies were on the left, 65 (45.1%) on the right, and 6 (4.2%) were midline. Based on the definition of anterior (including the symphysis and parasymphysis) and lateral (including the body, angle, ramus, and condyle of the mandible), 86 osteotomies were anterior (59.7%) and 58 lateral (40.3%). The osteotomy junction was differentiated by whether contact was between the MFTT and native mandible or between 2 segments of the MFTT. An overall 117 (81.2%) junctions were between the native mandible and MFTT, while 27 (18.8%) were between 2 MFTT bony segments. Bone union rates based on radiographic images were evaluated by 2 independent radiologists. Interrater reliability was measured via the kappa statistic. Weighted kappa statistics for interrater reliability showed substantial agreement (0.73; 95% CI, 0.63-0.82). Each radiologist's score was averaged.

A univariant analysis was done to determine correlation between bone union scores and several variables (**Table 3**). Age (OR = 0.99, P = .346) and smoking (OR = 0.73, P = .484) did not correlate with lower bone union scores. Lower bony union score was not significantly associated with preoperative (OR = 0.50, P = .217) or postoperative (OR = 0.49, P = .088) chemotherapy. Patients who underwent preoperative (OR = 0.30, P = .027) and postoperative (OR = 0.28, P = .003) radiation had a significantly lower bone union score than those without radiation. Lower bone union score was not associated with the length of osteotomy (OR = 0.97, P = .683) or site (OR = 0.79, P = .264). Lower bone union rates did not correlate with whether the free flap junction was between the native bone and osseous MFTT or between 2 osseous MFTT segments (OR = 0.88, P = .677). Time from surgery to postoperative imaging was associated with higher bone union scores (OR = 1.07, P = .024). The longer the duration from surgery to imaging, the higher the odds of a higher bone union score. Lower bone union scores did not appear to correlate with increased clinical complications (OR = 1.04, P = .940).

We compared bone union scores among types of MFTT (**Table 4**). With OCRFs as a reference, fibular (OR = 5.62, P = .008) and scapular (OR = 4.69, P = .043) MFTT had significantly higher bone union scores. Between fibular and

Table 3. Univariate Association Between Bone Union Scores and Possible Predictors.

	Odds ratio	95% CI	*P* value
Age	0.99	0.96-1.02	.3463
Smoking	0.73	0.31-1.75	.4840
Preoperative			
Radiation	0.3	0.1-0.87	.0265[a]
Chemotherapy	0.5	0.17-1.5	.2172
Postoperative			
Radiation	0.28	0.12-0.65	.0029[a]
Chemotherapy	0.49	0.22-1.11	.0879
Length of osteotomy	0.97	0.86-1.11	.6835
Osteotomy junction	0.88	0.48-1.62	.6766
Duration from surgery to CT scan	1.07	1.01-1.14	.0236[a]
Site	0.79	0.51-1.2	.2644
Clinical complication	1.04	0.34-3.18	.9403

Abbreviation: CT, computed tomography.
[a] $P < .05$.

Table 4. Odds Ratios and Comparison of Bone Union Based on Microvascular Free Tissue Transfer Type.

Free flap	Odds ratio	95% CI	*P* value
Fibula vs OCRF	5.62	1.58-20	.0077[a]
Scapula vs OCRF	4.69	1.05-21	.0432[a]
Scapula vs fibula	1.20	0.39-3.65	.7501

Abbreviation: OCRF, osteocutaneous radial forearm.
[a] $P < .05$.

scapular MFTT, there was no significant difference in bone union scores (OR = 1.20, $P = .7501$).

Furthermore, we examined patients who developed clinical complications of the mandibular reconstruction site postoperatively. There did not appear to be any statistically significant correlation between clinical complications and various variables (**Table 5**). Interestingly, the type of free flap did not appear to be associated with increased clinical complications.

Discussion

MFTT has become the mainstay treatment for major head and neck reconstructions and is frequently used in conjunction with segmental mandibulectomies for osseous reconstruction of the mandible. Osseous MFTT has become the gold standard of care for ensuring postoperative functionality and aesthetics. Previous studies have shown that there are comparable rates of postoperative morbidity, mortality, and functionality among the most common types of osteocutaneous free flaps: the radius, fibula, and scapula.[8] The data regarding bone union and its correlation with complications are lacking. In this study, we examined bone union scores following mandibular reconstruction based on postoperative imaging and their association with patient characteristics, free flap type, and surgical features. We also evaluated whether any variables, including bone union scores, correlated with postoperative complications.

Exposure to radiation has been reported to be a factor associated with impaired wound healing in MFTT.[9-12] The mechanism of this impact can be attributed to increased inflammation in response to tissue damage, which can subsequently result in a dysregulated healing process, abnormal collagen deposition, and fibrosis.[13] Previously irradiated tissue also displays hypercoagulability and impaired vascularity, which contribute to its hypoxic and hypocellular nature.[14] In our data, patients who had undergone pre- and postoperative radiation had lower bony union scores. Previous literature has reported on the impact that radiation can have on wound healing and flap failure, demonstrating a dose-dependent reduction in bone-healing ability with radiation.[10,14] Animal studies performed by Takahashi et al revealed that nonirradiated bones displayed complete or nearly complete healing, whereas irradiated bones showed significantly less healing, with almost no possibility of healing above 50 Gy.[14] In contrast, Akashi et al cited a radiological bone union rate of 91% among fibular grafts in mandibular reconstruction after 2 years, regardless of radiation therapy.[5] These data support the notion that although irradiated tissue may be impaired, there is still a possibility of bone union with an extended timeline.[5] Our patients underwent postoperative imaging at a median

Table 5. Univariate Association Between Clinical Complications and Possible Predictors.

	Patients, No. (%) or median (Q1, Q3)		
	No (n = 46)	Yes (n = 12)	*P* value
Age, y	61 (49, 69)	56 (52, 64)	.6867
Sex			.4791
Female	14 (30.4)	2 (16.7)	
Male	32 (69.6)	10 (83.3)	
Smoking			.7326
No	16 (34.8)	3 (25)	
Yes	30 (65.2)	9 (75)	
Alcohol			.1012
No	29 (63)	4 (33.3)	
Yes	17 (37)	8 (66.7)	
Preoperative radiation			.1909
No	40 (87)	8 (66.7)	
Yes	6 (13)	4 (33.3)	
Preoperative chemotherapy			.1909
No	40 (87)	8 (66.7)	
Yes	6 (13)	4 (33.3)	
Postoperative radiation			>.9999
No	21 (45.7)	5 (41.7)	
Yes	25 (54.3)	7 (58.3)	
Postoperative chemotherapy			.7463
No	27 (58.7)	8 (66.7)	
Yes	19 (41.3)	4 (33.3)	
Duration from surgery to CT scan, mo	9.2 (5.6, 15.8)	11.9 (5.2, 14.6)	.9353
Length of osteotomy, cm	7 (6, 8)	7 (5, 12)	.8212
Free flap type			.0871
Fibula	37 (80.4)	7 (58.3)	
Scapula	4 (8.7)	4 (33.3)	
Osteocutaneous radial forearm	5 (10.9)	1 (8.3)	

Abbreviation: CT, computed tomography.

11.6 months after surgery, consistent with the conclusion that, over time, irradiated tissue could also display normal bone union.

We found that the longer the time from surgery to the postoperative CT scan, the higher the rate of successful bony union. While typical bone union occurs in approximately 6 weeks, previous research has shown that reconstructed mandible bone union occurs on a more extended timeline, with multiple studies showing upward of 90% bone union rates >4 years after surgery.[4,14] Our data follow previously established patterns of bone healing, demonstrating that it can take months for bone remodeling to regenerate normal bone structure and exhibit visible callus formation.[13] Given this extended timeline, it is understandable that increased time between surgery and postoperative imaging correlated with higher rates of bony union, as in our study.

Our study did not find any correlation between lower bone union scores and smoking history. This is similar to conclusions established from previous literature—namely, Tsang et al and Dean et al.[15,16] Interestingly, Chen et al and van Gemert et al both suggested that smoking is an independent risk factor for complications of bone fixation, specifically for late complications.[17,18] Toxic compounds found in cigarette smoke, such as nicotine and carbon monoxide, invoke a highly hypoxic and vasoconstrictive environment, thereby inhibiting the normal wound-healing processes and resulting in increased complications.[17]

In comparing bone union scores among types of MFTT, we found that the OCRF had a significantly lower score than fibular and scapular free flaps. These findings are consistent with conclusions in other studies. Blumberg et al reported rates of 74.4% to 82.6% for complete or partial bony union in a scapula free flap cohort.[19] Yla-Kotola et al cited a radiologic nonunion rate of 20% in their fibular free flap group.[6] OCRF nonunion rates in mandibular reconstruction range from 5% to 13.8%.[19-21] Radiographic nonunion of all evaluated osteotomies was 19.4% in the current study. This finding may be due in part to the method by which osteotomies are performed. Although the specific mechanism of mandibular osteotomy healing has not been reported, the biology of fracture healing has been examined.[20] Bone fractures undergo healing in a direct or indirect fashion. Most bone healing occurs indirectly, whenever there are gaps between bones. This process begins with an acute inflammatory response, leading to the generation of a primary cartilaginous callus. This callus then remodels to restore normal bone structure.[20,21] When bone segments are in direct contact, the remodeling step is bypassed, and lamellar bone and the haversian systems are immediately regenerated.[20] Although not specific to the mechanism of healing, Hashemi et al examined the optimal osteotomy gap distance on achieving bone union in fibular free flaps. This study revealed that the mean osteotomy gap size achieving union was 1.31 mm, while distances >2.55 mm correlated with higher risk of nonunion.[22]

In fibulas, closing osteotomies are routinely performed where the bone is cut to the exact angle of the mandibular junction. In contrast, at our institution and many others, opening osteotomies are performed in scapulas and OCRFs. During opening osteotomies, we perform a controlled osteotomy through the cortical bone and crack the bone to our desired length and angle. This method often leaves the bone in contact at the lingual aspect but a gap in the labial side. The difference in closing and opening osteotomies may contribute to the differences in rate of bony union among MFTT types. We hypothesize that this method may explain the lower bony union rates in OCRF in comparison with fibular free flaps. Most scapular free flaps done at our institution incorporate the scapular tip and a portion of the lateral boarder supplied by the angular artery. A possible explanation may be that bone harvested from scapulas often have robust muscular attachments that are adherent to the bone, such as the infraspinatus, subscapularis, and teres muscles. In contrast, the radius is often dissected down to the periosteum and has a more tenuous blood supply than the scapula. This additional tissue may help reinforce and provide progenitor cells, which may promote union. In support of this theory and the superior outcomes with scapular MFTT, Tsang et al displayed lower rates of hardware complications with scapular free flaps as compared with fibular free flaps.[15] Their conclusion was attributed to the abundance of soft tissue present in a scapula free flap, its long vascular pedicle, as well as the ability for patients to immediately ambulate following reconstruction with a scapula free flap, unlike with a fibula free flap.[15] In our study, fibular and scapular free flaps were comparable in bone union scores.

The significance that radiographic bony union has on complication rates has yet to be uncovered. However, there have been multiple studies exploring MFTT and the development of hardware-related complications.[15,16] Plate-related complications range from 12% to 36.4% and include exposed plate or bone, loosening of screws, fistulas, and bone resorption.[16,23] These studies defined nonunion as a complication, rather than examining how bony union correlated to complications. Results in our study showed a clinical complication rate of 20.7%. In our findings, the type of free flap used was not associated with a difference in complication rates. In a retrospective single-institution comparison among OCRF, fibular, and scapular free flaps, Militsakh et al found similar rates of microvascular failure, defined as complete loss of soft and/or bony portions of the flap. The authors also noted that functional outcomes, such as diet, tracheostomy dependence, and dental rehabilitation, were similar between the groups.[24] In contrast, a retrospective multicenter cost-comparison analysis among types of MFTT revealed that OCRF had the lowest complication rate, length of stay, duration of operation, and charges of hospitalization.[25] In our study, the complication rate did not appear to be associated with bony union. These findings suggest that radiographic bony union may not necessarily predict flap compromise or poor clinical outcome.

Conclusion

Osseous MFTT is the mainstay of segmental mandibular reconstruction. Our results demonstrate that radiation and time from surgery both have an impact on bone union. Regarding type of MFTT, fibular and scapular MFTT appeared to have higher bone union scores when compared with OCRF. We hypothesize that this difference is due to our method of reconstruction, including closing vs opening osteotomies. Interestingly, clinical complications did not appear to correlate with MFTT type or bone union scores. To our knowledge, this is the first study to examine the 3 most frequently used types of osseous MFTT in mandibular reconstruction and assess bone union as well as clinical outcomes. Larger and longer-term prospective studies would be valuable in guiding our approach to osseous MFTT in mandibular reconstruction.

Author Contributions

Akina Tamaki, design, acquisition of data, analysis and interpretation of data; **Shruthi Sethuraman**, acquisition of data, analysis and interpretation of data; **Lucy Shi**, acquisition of data, analysis and interpretation of data; **Songzhu Zhao**, analysis and interpretation of data; **Keith C. Carver**, acquisition of data; **Angel Hatef**, acquisition of data; **Michael Luttrull**, acquisition of data; **Nolan B. Seim**, design, analysis and interpretation of data; **Stephen Y. Kang**, design, analysis and interpretation of data; **Enver Ozer**, design, analysis and interpretation of data; **Amit Agrawal**, design, analysis and interpretation of data; **Matthew O. Old**, design, analysis and interpretation of data.

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